REMARKS

The non-elected claims 3-20, 22 and 24 and claim 23 have been canceled without prejudice. Claims 1 and 21 have been amended. Claims 1, 2 and 21 are pending and at issue.

Claim 1 and 21 have been amended to replace the term "insect" in step (i) with "*Tenebrio molitor* or *Holotrichia diomphalia*". Support for this amendment can be found in Examples 1 and 4 of the specification.

No new matter has been introduced by these amendments. Entry and consideration of the amendments is therefore respectfully submitted.

Rejections Under 35 U.S.C. § 102(b), Should Be Withdrawn

Leonard Reference:

Claims 1, 2, 21 and 23 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Leonard et al. (Insect Biochem, Vol. 15, No. 6, pp. 803-810).

Claim 23 has been canceled without prejudice.

Leonard discloses fractions obtained from haemocyte lysate of *Blaberus craniifer* exhibiting phenoloxidase activity (see, Table 1 of the Leonard reference). Leonard does not disclose a mixture of plasma and hemocyte lysate from *Tenebrio molitor* or *Holotrichia diomphalia* exhibiting phenoloxidase activity as called for in claim 1. Claim 21 calls for lysate treated *Tenebrio molitor* or *Holotrichia diomphalia* plasma fractions exhibiting phenoloxidase activity. Leonard does not disclose a composition comprising lysate treated *Tenebrio molitor* or *Holotrichia diomphalia* plasma fractions. Accordingly, the subject matter of claims 1, 2 and 21 of the present application is novel over Leonard.

Asokan Reference:

Claims 1 and 21 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Asokan et al. (Dev. And Comp. Immun., Vol. 21, No. 1, pp 1-12).

Asokan discloses phenoloxidase activity in plasma and haemocytes of the marine mussel *Perna viridis* (see Abstract of the Asokan reference). Asokan also discloses prophenoloxidase (proPO) enzyme in insect and crustacean haemocytes, plasma or in both plasma and haemocyte fractions (see page 2, column 1 of the Asokan reference).

There are several differences between the presently claimed invention and Asokan. First, Asokan does not disclose a composition comprising a mixture of plasma and haemocyte lysate or lysate treated plasma from *Tenebrio molitor* or *Holotrichia diomphalia* exhibiting phenoloxidase activity as called for in claims 1 and 21.

Applicants respectfully submit that "phenoloxidase" and "prophenoloxidase" as disclosed in Asokan are two different enzymes. Asokan distinguishes phenoloxidase (PO) and prophenoloxidase (proPO) enzymes as stated below:

> "In arthropods, PO exists in haemolymph as an inactive enzyme, prophenoloxidase (proPO), which is activated to PO by both an endogenous activating system and exogenous reagents such as lipids, detergents and organic solvents (4-7)." See page 1, column 2 of the Asokan reference.

Asokan only discloses prophenoloxidase (proPO) enzyme in insect and crustacean plasma and haemocyte fractions and fails to describe a composition from *Tenebrio molitor* or *Holotrichia diomphalia* exhibiting phenoloxidase activity as called for in the claimed invention.

Second, *Tenebria molitor* and *Holotrichia dimophalia* of the claimed invention exhibit surprisingly high phenoloxidase levels compared to other insects, i.e., *Drosophila melangaster* and *Galleria mellonella* upon treatment with β-1,3-glucan. See Exhibit A, red bars. This result may be due to *Tenebria molitor* and *Holotrichia dimophalia*'s relatively large larva size compared to other insects. The larger size larva enables easier and larger-scale extraction of hemoloymph and as a result increased phenoloxidase activity.

This result may additionally be attributed to the fact that the initially collected hemolymph of *Tenebrio molitor* and *Holotrichia diomphalia* show lower phenoloxidase activity compared to hemolymph from other insects, i.e., *Drosphila melangaster* and *Galleria mellonella.* See Exhibit

A, yellow bars. This initial sample from *Tenebrio molitor* and *Holotrichia diomphlia* contains prophenoloxidase (proPO) which is activated to phenoloxidase upon treatment with β-1,3-glucan. It is advantageous to have low phenoloxidase activity-which indicates that the enzyme is in its inactive form (proPO)-prior to treatment with β-1,3-glucan.

Asokan clearly does not disclose a composition comprising a mixture of plasma and haemocyte lysate or a lysate treated plasma from *Tenebrio molitor* or *Holotrichia diomphalia* as discussed above. At best, Asokan describes prophenoloxidase (proPO) enzyme in insect and crustacean plasma and haemocyte fractions.

For the foregoing reasons, claims 1 and 21 are not disclosed by Asokan and withdrawal of this ground for rejection is believed to be in order.

The Examiner quires about claim 23 regarding how it further limits claim 2 from which it depends. Claim 23 has been canceled without prejudice.

Rejections Under 35 U.S.C. § 103(a), Should Be Withdrawn

Claims 2 and 23 are rejected under 35 U.S.C. § 103(a) as obvious over the combination of Asokan in view of Ashida.

Claim 23 has been canceled without prejudice.

The Examiner alleges that the present claim 2, which states detecting glucans at concentrations as low as 20 pg/ml, reads on concentrations higher than 0.1 ng/ml, as disclosed in the Ashida reference.

The Asokan reference has been discussed, *supra*, in connection with the rejections over 35 U.S.C. § 102(b). Asokan discloses phenoloxidase activity in plasma and haemocytes of the marine mussel *Perna viridis* and prophenoloxidase (proPO) enzyme in insect and crustacean haemocytes, plasma or in both haemocyte and plasma fractions. Asokan does not teach or suggest a composition comprising a mixture of plasma and hemocyte lysate from *Tenebrio molitor* or *Holotrichia diomphalia* exhibiting phenoloxidase activity. Moreover, Asokan does not teach or suggest the detection sensitivity of the presently claimed fractions.

Ashida does not overcome the deficiencies of Ashida. In particular, the compositions of Ashida have limited sensitivity and can only detect β-1,3-glucan concentrations higher than 0.1 ng/ml (see Fig. 3 on sheet 2 of 4 of Ashida). By contrast, the composition of claim 2 can detect β-1,3-glucan concentrations as low as 20 pg/ml. This is surprising and entirely unexpected.

It is respectfully submitted that the present invention has superior sensitivity for detecting β-1,3-glucan. A skilled person could not have expected these improved properties without the benefit of the teachings in the present application, even upon considering the combined teachings of Asokan and Ashida. For this reason, the present claims are not obvious over Asokan in view of Ashida and this rejection should be withdrawn.

Conclusion

In light of the above mentioned amendments and arguments, all of the pending claims in this application are believed to be in condition for allowance. Entry and consideration of these amendments and remarks are therefore respectfully requested. The Examiner is invited to contact Applicants' representative at the below-indicated telephone number if he believes it would advance prosecution of the application. An allowance is earnestly sought.

Dated: April 29, 2004

Respectfully submitted,

By _____

S. Peter Ludwig
Registration No.: 25, 351
DARBY & DARBY P.C.
P.O. Box 5257
New York, New York 10150-5257
(212) 527-7700
(212) 753-6237 (Fax)
Attorney For Applicant